Articles

Prognosis of Mechanically Ventilated Patients

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In this Department of Veterans Affairs cooperative study, we examined predictors of in-hospital and 1-year mortality of 612 mechanically ventilated patients from 6 medical intensive care units in a retrospective cohort design. The outcome variable was vital status at hospital discharge and after 1 year. The results showed that 97% of patients were men, the mean age was 63 ± 11 years (SD), and hospital mortality was 64% (95% confidence interval, 60% to 68%). Within the next year, an additional 38% of hospital survivors died, for a total 1-year mortality of 77% (95% confidence interval, 73% to 80%). Hospital and 1-year mortality, respectively, for patients older than 70 years was 76% and 94%, for those with serum albumin levels below 20 grams per liter it was 92% and 96%, for those with an Acute Physiology and Chronic Health Evaluation II (APACHE II) score greater than 35 it was 91% and 98%, and for patients who were being mechanically ventilated after cardiopulmonary resuscitation it was 86% and 90%. The mortality ratio (actual mortality versus APACHE II-predicted mortality) was 1.15. Conclusions are that patient age, APACHE II score, serum albumin levels, or the use of cardiopulmonary resuscitation may identify a subset of mechanically ventilated veterans for whom mechanical ventilation provides little or no benefit.

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Determining the prognosis of a patient who receives mechanical ventilation is essential to physicians, patients, and families who are trying to make informed decisions about the appropriateness of life-sustaining therapy. About 20% of patients in medical intensive care units (ICUs) receive mechanical ventilation,[1] the highest level of ICU support.

Previous outcome studies of medical patients treated with mechanical ventilation have been done primarily in university and community hospitals and have noted mortality rates between 50% and 60%.[2,3]* It is uncertain whether these results would apply to hospitals operated by the Department of Veterans Affairs (VA), the single largest health care system in the country and where more than a third of physicians in residency training receive their education.[4]

*See also the editorial by W. A. Knaus, MD, "Predicting Outcome From Mechanical Ventilation," on pages 700-702.

Our previous work suggested that it was possible to identify factors associated with poor survival in veterans who are being mechanically ventilated.[5] These included low serum albumin levels, a high fractional inspired oxygen (FIO_2) concentration after 24 hours on the ventilator, and a high score on the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system for severity of illness of patients in ICUs. We undertook this cooperative study to validate these findings and to examine the performance of APACHE II in VA medical centers.

Patients and Methods

Setting and Patients

We did a retrospective cohort study at six VA medical centers: Durham, North Carolina; San Antonio, Texas; Seattle, Washington; West Haven, Connecticut; Long Beach, California; and Palo Alto, California. All six centers are major teaching hospitals of affiliated university

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ABBREVIATIONS USED IN TEXT

APACHE II = Acute Physiology and Chronic Health Evaluation II
CI = confidence interval
CPR = cardiopulmonary resuscitation
Fio_2 = fractional inspired oxygen
ICU = intensive care unit
Pco_2 = partial pressure of carbon dioxide (tension)
VA = Department of Veterans Affairs

medical schools. All medical patients who received mechanical ventilation during a one- or two-year period (January 1, 1986, to December 31, 1987) were included. Patients were identified from the ICU logs. We excluded patients who were recovering from surgical procedures; those who had been admitted to the ICU primarily for the treatment of a cardiac disorder, such as myocardial infarction or congestive heart failure; or those who had a diagnosis of acquired immunodeficiency syndrome. We also excluded 13 patients who were on long-term ventilatory support at the time of admission to the ICU. For patients with many admissions to the hospital during the study period that required mechanical ventilation, one admission was randomly chosen for inclusion in the study. (In all, 22 patients had two such hospital admissions, and 2 patients had a collective total of nine such admissions). Medical records were available for 88% of eligible patients. These 612 patients constitute the sample for this study.

Data Collection Procedures

Patients were identified at each site from ICU and respiratory care logs. Medical records from the sites were sent to the study coordinating center at the San Francisco, California, VA Medical Center for data abstraction. Chart data were supplemented from on-site computers and laboratory records.

Measurements

Predictor variables. We hypothesized that the following variables would be associated with mortality: advanced age, the use of cigarettes, the use of alcohol, low serum albumin levels, low total lymphocyte counts at the initiation of mechanical ventilation, the initiation of mechanical ventilation after cardiopulmonary resuscitation (CPR), abnormal arterial blood gas values after 24 hours of ventilation, and prolonged duration of mechanical ventilation, ICU, and total hospital stay. Serum albumin levels within a day of the initiation of mechanical ventilation were recorded. (One medical center's routine serum chemistry panel did not include serum albumin levels.) Diagnoses were taken from the discharge summary, patient progress notes, or autopsy report, if available. Repeated episodes of mechanical ventilation during one hospital stay were counted as one unit of observation, and the total days of ventilation were summed. Cardiopulmonary arrest was defined as the cessation of both cardiac and respiratory function.

The APACHE II scoring system, a severity of illness measurement with higher scores associated with higher mortality, was used to compute the predicted death rate for the group.[2] Data for APACHE II were collected for the first 24 hours of an ICU admission. We also calculated a modified APACHE II score that excluded age.

Outcome variable. Determinations of vital status at hospital discharge and at one year were made from the medical records, coroner's report, or the National Death Index.

Analysis

Continuous data were compared by Student's t test. Categorical data, including binary data, were tested by the χ^2 statistic. Comparisons with a P value of less than 5% (2-tailed) were designated as statistically significant. Logistic regression analyses were used, and the dependent variable was whether the patient was discharged from the hospital (alive). Independent variables include age, serum albumin levels, and APACHE II score. Not every patient had the serum albumin level recorded; those analyses involving serum albumin were done with a reduced data set. Proportional hazards models were used to determine the predictors of one-year mortality.

Results

Most patients were older men (Table 1); 23% were older than 70 years. Smoking and excessive alcohol use were common. Primary diagnoses for admission to an ICU are shown in Table 2. The most common were infection and chronic obstructive pulmonary disease.

In all, 64% of the patients died during the hospital stay (95% confidence interval [CI], 60% to 68%). Within the next year, an additional 84 patients had died (38% of hospital survivors), for a total one-year mortality of 77% (95% CI, 73% to 80%). Mortality rates by diagnoses are

TABLE 1.—*Characteristics of 612 Mechanically Ventilated Medical Patients**

Characteristic	*No. of Patients or Results*	*%*
Male sex	595	97
Age, years	63.3 ± 10.8	--
APACHE II score	26.6 ± 9.2	--
Days in hospital	28.4 ± 38.6	--
Days in ICU	10.8 ± 33.7	--
Days ventilated	7.5 ± 15.1	--
Mean serum albumin level, grams/liter	30.0 ± 7.5	--
Cigarette use		
Ever	503	94
Pack-years	68.7 ± 57.4	--
Current	248	48
Packs/day	1.5 ± 1.4	--
Unknown	75	12
Excessive alcohol use		
Ever	382	78
Current	168	31
Drinks/day	9.7 ± 7.3	--
Unknown		20

ICU = intensive care unit

*Plus-minus values are means ± standard deviation.

TABLE 2.—*Primary Reason for Admission to a Medical Intensive Care Unit*

Diagnosis	Patients, No. (%)	Mortality, No. (%) Hospital	1-Year
Sepsis	90 (15)	67 (74)	77 (86)
Infection	89 (14)	48 (54)	62 (70)
Chronic obstructive pulmonary disease	85 (14)	30 (35)	51 (60)
Postcardiac arrest	47 (8)	42 (89)	44 (94)
Gastrointestinal bleeding	45 (7)	39 (87)	42 (93)
Postrespiratory arrest	42 (7)	22 (52)	28 (67)
Aspiration	39 (6)	28 (72)	34 (87)
Neoplasm	29 (5)	23 (79)	26 (90)
Gastrointestinal organ system	24 (4)	19 (79)	20 (83)
Neurologic organ system	22 (4)	18 (82)	19 (86)
Seizure disorder	17 (3)	11 (65)	14 (82)
Respiratory organ disease or other	20 (3)	10 (50)	14 (70)
Intracranial hemorrhage	15 (2)	13 (87)	14 (93)
Drug overdose	14 (2)	0 (0)	2 (14)
Metabolic or renal organ disease	13 (2)	9 (69)	11 (85)
Hemorrhagic shock or hypovolemia	10 (2)	6 (60)	9 (90)
Pulmonary embolus	7 (1)	5 (71)	6 (86)
Asthma	3 (1)	0 (0)	0 (0)
Missing information	1 (0)	1 (100)	1 (100)
Total	612 (100)	391	474

listed in Table 2. There were too few patients with any single diagnosis to determine whether the diagnosis was an independent predictor of outcome; patients with drug overdose, however, had substantially better survival.

Variables Associated With In-hospital Mortality

All variables associated with mortality in univariate analyses (at $P < .05$) are shown in Table 3. Patients who died during the hospital admission had shorter hospital stays (25.5 ± 32.5 days [SD] compared with 33.6 ± 47.2 days, $P = .01$) but a longer duration of mechanical ventilation (8.6 ± 17.1 days compared with 5.6 ± 10.5 days, $P = .004$). Nearly two fifths of nonsurvivors (38%) and 25% of survivors received mechanical ventilation for more than five days ($P < .01$). Arterial blood gas values 20 to 24 hours after mechanical ventilation was initiated in survivors and nonsurvivors still on respirators were similar except for the arterial carbon dioxide pressure (Pco_2), which was significantly higher in survivors (38.8 ± 9.4 mm of mercury compared with 35.3 ± 11.2 mm of mercury, $P < .01$). The Pco_2 was not a good predictor of mortality, however. A third of patients (n = 28) who were receiving an Fio_2 concentration of greater than 50% at 24 hours survived their hospital stay. Increasing age and APACHE II score, lower serum albumin levels, and mechanical ventilation being initiated after CPR were all associated with increased in-hospital mortality (Tables 3 and 4).

Age. Survivors tended to be younger. Hospital mortality among the elderly (>70 years old) was 75% compared with 60% in those younger than 70 years (Tables 3 and 4).

Serum albumin. The serum albumin level had a strong association with hospital mortality (Tables 3 and 4). The hospital mortality for patients with serum albumin levels of less than 25 grams per liter was 82%. Of the two patients with serum albumin levels of less than 20 grams per liter who survived the period in the hospital, one died six weeks after hospital discharge. Of patients with serum albumin levels below 25 grams per liter who died in the hospital, 44% did so within five days of the initiation of mechanical ventilation.

To determine whether serum albumin levels obtained after the initiation of mechanical ventilation were useful in predicting outcome, we examined the variation in serum albumin levels over three consecutive days and found that it was large. In 39 patients in whom serum albumin levels were available on the day preceding, the day of, and the day following the initiation of mechanical ventilation, the mean serum albumin levels fell from 31 to 26 grams per liter. A total of 255 patients had a serum albumin level measured 24 hours after mechanical ventilation was initiated. Of these patients, 60 had serum albumin values below 25 grams per liter, with a hospital and one-year mortality of 75% and 83%, respectively. Patients with serum albumin levels above 25 grams per liter had a hospital and one-year mortality of 57% and 74%, respectively.

To determine whether the serum lymphocyte count could be used as a predictor of outcome for patients in whom serum albumin levels are unavailable, we examined the correlation between the serum albumin level and the absolute lymphocyte count in the three days surrounding mechanical ventilation and found none (correlation coefficient, $-.12$, $-.12$, and $+.13$, respectively).

We determined how many patients with serum albumin levels below 25 grams per liter would meet previously published criteria for a lack of benefit from total parenteral nutrition.[6] We found that 57% of these patients had an APACHE II predicted mortality of greater than 60%, with an actual mortality of 88%. The hospital mortality rate in the remaining patients with serum albumin levels below 25 grams per liter was 71%.

APACHE II score. Higher APACHE II scores were associated with increased hospital mortality (Tables 3 and 4 and Figure 1); 90% of patients with APACHE II scores greater than 35 died in the hospital. Because age is a component of the APACHE II score,[2] we examined age and APACHE II score without age (modified APACHE II) in multivariate models. Each was an independent predictor of outcome.

Cardiopulmonary resuscitation. Patients who were placed on mechanical ventilation after receiving CPR had a hospital mortality of 86% (Tables 3 and 4). None of the 13 patients aged 70 years or older survived the period in hospital when placed on mechanical ventilation after CPR (95% CI, 0% to 28%).

Variables Predictive of One-Year Mortality in Hospital Survivors

Age, APACHE II score, and modified APACHE II score were independent predictors of mortality in the year

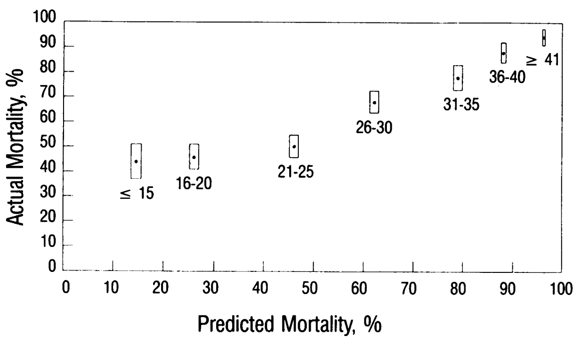

Figure 1.—A calibration chart shows mortality ratios by Acute Physiology and Chronic Health Evaluation II scores. The box around each point indicates standard deviations in both dimensions.

after hospital discharge (Tables 3 and 4). Among those patients who survived their hospital stay, 38% younger than 70 years died within the first year after hospital discharge, for a total one-year mortality of 75%. Of the survivors older than 70 years, 76% died in the year after hospital discharge, for a total one-year mortality of 94% in the geriatric population (95% CI, 88% to 97%). The total one-year mortality for patients whose APACHE II score was higher than 35 was 97% (95% CI, 91% to 99%).

Performance of the APACHE II System for Predicting In-hospital Mortality

The predicted group mortality based on the APACHE II risk equation was 55%, with a 64% actual mortality, for a mortality ratio (actual/predicted) of 1.15. Individual hospital mortality ratios ranged from 0.9 to 1.4. Mortality ratios were also analyzed based on categories of APACHE II scores (Figure 1). With APACHE II scores greater than 20, mortality ratios approached 1 at all hospitals. With APACHE II scores of less than 20, the mean mortality ratio was 2.0 (range 1.0 to 3.1) and was greater than 1.3 in five of the six hospitals (mean 2.3 in the 5 hospitals).

In 17 patients with APACHE II scores of less than 20 and serum albumin levels of less than 25 grams per liter, the hospital mortality was 76%, higher than would have been predicted based on the APACHE II score alone. We used APACHE II scores and serum albumin values in a logistic regression model to predict mortality. As expected, the mean mortality ratio for APACHE II scores of less than 20 improved to 1.2 and approached 1.0 for APACHE II scores of greater than 20. (The following logistic regression equation was used: $Q = -0.86 - [0.08 \cdot \text{APACHE II score}] + [0.73 \cdot \text{serum albumin level from day preceding or of mechanical ventilation}]$, where Q is the natural logarithmic odds of mortality.)

Discussion

The in-hospital mortality for medical patients who received mechanical ventilation in the six VA medical centers in our study was 64%. Of those who survived the period in the hospital 38% died within the first year, bringing the total one-year mortality to 77%. Mortality was even higher among patients older than 70 years: three in four of these patients died during the initial hospital stay, and the one-year mortality was 94%. Four variables were independently associated with increased in-hospital

TABLE 3.—*Variables Associated With In-hospital Mortality and, for Those Patients Who Survived Hospital Admission, 1-Year Mortality*

	In-hospital Mortality				*1-Year Mortality*			
Variable	*No.*	*Odds Ratio*	*(95% CI)*	*P Value*	*No.*	*Hazard Ratio*	*(95% CI)*	*P Value*
Univariate Model								
Days in hospital/day increase	611	0.99	(0.99-1.00)	.02	220	1.0	(1.0-1.0)	.57
Days ventilated/day increase	607	1.02	(1.00-1.04)	.02	219	1.0	(1.0-1.0)	.59
Age/10-year increase	612	1.3	(1.1-1.6)	<.001	220	1.8	(1.4-2.1)	<.001
Serum albumin level/ 10 grams-per-liter decrease	320	2.3	(1.6-3.2)	<.001	105	1.1	(0.7-1.5)	.79
APACHE II score/10 point increase	571	2.7	(2.1-3.5)	<.001	210	1.8	(1.4-2.4)	<.001
Modified APACHE II score*	571	2.6	(2.1-3.4)	<.001	210	1.7	(1.3-2.2)	<.001
Cardiopulmonary resuscitation	606	3.9	(2.1-7.3)	<.001	219	0.6	(0.2-1.5)	.25
Pco_2/5 mm-of-mercury decrease	309	1.2	(1.1-1.3)	.007	127	1.0	(0.9-1.1)	.66
Multivariate Models								
Model 1								
Serum albumin level/ 10 grams-per-liter decrease	308	2.1	(1.5-3.1)	<.001	101	1.0	(0.7-1.4)	.81
Modified APACHE II score*	308	2.2	(1.5-3.1)	<.001	101	1.2	(0.7-1.9)	.56
Age/10-year increase	308	1.2	(1.0-1.5)	.129	101	1.8	(1.3-2.6)	<.001
Model 2								
Modified APACHE II score*	571	2.6	(2.0-3.3)	<.001	210	1.6	(1.2-2.1)	.001
Age/10-year increase	571	1.3	(1.1-1.6)	.001	210	1.9	(1.5-2.3)	<.001

APACHE II = Acute Physiology and Chronic Health Evaluation II, CI = confidence interval, Pco_2 = partial pressure of carbon dioxide.

*Per 10-point increase.

TABLE 4.—*Variables Associated With In-hospital and 1-Year Mortality*

		In-hospital			1-Year		
Variable	*No.*	*No. Dead*	*(%)*	*(95% CI)*	*No. Dead*	*(%)*	*(95% CI)*
Age, years							
<60	180	108	(60)	53-67	127	(71)	64-77
60-69	294	178	(61)	55-67	230	(78)	73-82
70-79	113	86	(76)	67-83	106	(94)	87-97
80-89	21	16	(76)	52-91	20	(95)	74-100
>89	4	3	(75)	22-99	4	(100)	40-98
Serum albumin level, grams/liter							
<20	24	22	(92)	72-99	23	(96)	77-100
20-25	48	37	(77)	62-87	41	(85)	71-93
26-30	81	59	(73)	62-82	67	(83)	73-90
>30	167	97	(58)	50-66	126	(75)	68-81
APACHE II score							
≤15	50	22	(44)	29-59	28	(56)	41-71
16-20	104	48	(46)	36-56	63	(61)	51-71
21-25	129	64	(50)	41-59	98	(76)	67-83
26-30	110	75	(68)	59-77	97	(88)	80-93
31-35	73	57	(78)	66-86	66	(90)	80-95
36-40	57	50	(88)	76-95	54	(95)	85-99
>40	48	45	(94)	82-98	48	(100)	91-100
Cardiopulmonary resuscitation							
Yes	83	71	(86)	76-92	75	(90)	81-95
No	523	316	(60)	56-64	406	(78)	74-81

APACHE II = Acute Physiology and Chronic Health Evaluation II, CI = confidence interval

mortality: age, serum albumin levels, APACHE II scores, and the initiation of mechanical ventilation after CPR.

Many older veterans received mechanical ventilation; nearly a quarter of our patients were older than 70. Several studies have shown that age is a predictor of disability or death from mechanical ventilation.[7,8] We also found that advancing age increased the risk of dying in hospital and the one-year mortality.

Our findings confirm previous ICU studies showing that the serum albumin level is an important prognostic variable.[5,9-12] Hospital mortality for patients with serum albumin levels of less than 25 grams per liter was more than 80%, with a one-year mortality approaching 90%. The one-year mortality rose to 96% if the serum albumin level was below 20 grams per liter.

One can argue that a low serum albumin level should be used as a predictor of a poor prognosis only if an improvement in nutrition does not improve the patient's condition, yet the benefit of parenteral nutrition remains controversial.[13] It would be problematic to extrapolate results from the recent VA cooperative study on the role of total parenteral nutrition in surgical patients to our medical patients.[13,14] Also, nearly half of our patients with hypoalbuminemia who died did so within five days of the initiation of mechanical ventilation, making it unlikely that aggressive alimentation would have affected the outcome. Other investigators have used APACHE II scores to differentiate ICU patients who would not benefit from total parenteral nutrition.[6] These include patients with at least a 60% risk of death after ICU admission. In all, 57% of our patients with a serum albumin level of less than 25 grams per liter met this criterion. Further studies on the role of nutritional intervention would be useful.

Several nutritional studies have shown a correlation between serum lymphocyte counts and serum albumin levels.[15] We looked at whether the absolute lymphocyte count could be used as a prognostic variable if serum albumin levels were unavailable, but could show no correlation of serum lymphocyte counts to serum albumin levels or to mortality rate.

In our study, veterans who were placed on mechanical ventilation after CPR had the same 14% survival rate as was seen among patients who received CPR in a university hospital.[16] Elderly patients are least likely to benefit from CPR.[17] As in a study from the Houston VA Medical Center, none of our hospital survivors were older than 70 years.[18]

Our study confirms that the APACHE II scoring system performs well in predicting outcome for individual hospitals and the group as a whole among veterans receiving intensive care who are mechanically ventilated. Mortality ratios (actual to predicted mortality) based on APACHE II scores have been used to evaluate results in ICUs.[19] Among our sickest patients (APACHE II scores greater than 20), the observed hospital death rates were consistent with those predicted from APACHE II, suggesting that the quality of care was acceptable in VA medical centers. At APACHE II scores of below 20, however, actual mortality exceeded predicted mortality in five of six hospitals. There are at least two explanations for this calibration discrepancy. The first is that the discrepancy is due to a poor quality of care. The increased mortality ratios were seen in five of the six hospitals for the low scores, but in none of the six for higher APACHE II scores. The second explanation for the calibration discrepancy is selection bias. Our study protocol focused only on the "sickest" patients, whereas the APACHE system is based on all ICU patients. This differential selection may explain the higher hospital mortality ratios in our mechanically ventilated patients with low APACHE II scores. Knaus and co-workers showed a similar rise in predicted death rates when focusing on a special group that differs in case selection from the original APACHE II method.[1] Others have found increased mortality ratios in patients with complications (unintended, harmful occurrence resulting from a therapeutic intervention) and those not admitted to an ICU directly from an emergency department.[20,21] This study has identified an additional category of discrepant mortality ratios, that being ventilated medical patients with APACHE II scores of less than 20. Nonetheless, these discrepancies do not reduce the usefulness of the APACHE II scoring system, as it discriminates well, especially at the higher ranges where most of these mechanically ventilated patients scored.

We could not validate the clinical usefulness of arterial blood gas values after the initiation of mechanical ventilation for predicting outcome.[5] Hypocarbia or an Fio_2 of greater than 50% after 24 hours has previously been associated with a poor prognosis.[5,22] Although these variables were found statistically more frequently in our nonsurvivors, as many as a third of patients with these values survived the period in the hospital.

This study has several limitations. Data were obtained from chart review. Postoperative patients or those admitted to the ICU primarily for the treatment of a cardiac disorder were excluded from the study. We may have underestimated the frequency of current alcohol abuse or cigarette use. Serum albumin levels were missing in half the patients. Data on the primary diagnosis were missing in a few patients for whom only parts of the medical record were available. Vital status at hospital discharge and after one year were available in all patients, however. Last, this study in veterans may not be generalizable to patients in other settings.

This study does not answer the question of who will and who will not benefit from mechanical ventilation, but it does identify a subset of this relatively homogeneous population in whom mechanical intervention has a poor outcome and is possibly futile. Although there is no agreement on what constitutes futility or a level of prognosis poor enough to urge withholding intervention,[23-27] a one-in-ten chance of survival may be adequate justification for the continued use of ICU resources, but may be unacceptable if resources become scarcer. We hope these findings aid clinicians, patients, and families in making decisions about this life-sustaining therapy.

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